探討 HNMT 在神經膠質瘤生長中所扮演的角色

Study of histamine-N-methyltransferase (HNMT) in the glioma

中文摘要

神經膠質瘤源於神經膠細胞，其數量占大腦細胞的百分之九十，功能為分泌神經成長因子誘發神經纖維生長、形成髓鞘及血腦屏障。最常見的神經膠質瘤為神經膠母細胞瘤，神經膠質瘤形成的因素至今尚未完全明朗。由於神經膠質瘤生長邊界不明確，以手術方式無法清除乾淨，對於化學治療及放射線治療具有高度的抵抗性而不易治療。另一方面，因為神經膠質瘤的高度入侵性及致死率，使得科學家們致力於去開發及尋找新的治療方法及治療標的基因。之前研究發現同時給予 interlukin-2 (IL-2)及組織胺治療能有效地抑制惡性神經膠質瘤的生長及血管新生，這也暗示著組織胺有抑制神經膠質瘤生長的功能。組織胺在細胞內主要藉由 histamine-N-methyltransferase (HNMT)來代謝。前人的實驗結果已經證實組織胺含量及其代謝物和癌症有著一定的相關性，然而卻沒有相關的文獻直接指出 HNMT 和神經膠質瘤的關係或探討 HNMT 相關的致病機轉，本論文發現不論是神經膠質瘤組織或細胞株，HNMT 的表現量都較正常腦組織多，高度表現的 HNMT 暗示著抗癌的組織胺含量下降。另一方面，神經膠質瘤促進因子之一的 epithelial growth factor (EGF)會增加 HNMT 的表現及 HNMT 在細胞中位置的轉移。針對致命的神經膠質瘤，我們的結果提供 HNMT 是另一個新的治療標的。

英文摘要

Giloma derive from glial cell, which contribute about 90% of brain cells. The functions of glial cells are offering support and nutrition, forming myelin sheath and blood brain barrier.The most common glioma is glioblastoma multiforme (GBM) and the possible causes are not fully understood. Neurosurgery unable to remove the glioma from normal brain clearly；Glioma even resisten to high dose of radiotherapy and chemotherapy. The prognosis of malignant glioma remains dismal and the estimated median survival time is <1 year.It is emergent to develop new therapic policy and find out target genes. Previous data investigate that cotreatment with interleukin-2 (IL-2) and histamine inhibits growth and angiogenesis in malignant glioma. It also suggests that histamine has function of tumor suppression. In cytosol, histamine is metabolized by histamine-N- methyltransferase (HNMT). The concentration of histamine and its products have association with glioma. However, there is no direct evidence to investigate the roles of HNMT in growth and pathogenesis of glioma. Our data demonstrate that either specisement of GBM or glioma cell lines express more HNMT than normal brain tissue. More amount of HNMT suggests less tumorspressive histamine. On the other hands, we also find that

epidermal growth factor (EGF), a glioma inducing factor, increases the expression of HNMT and changes the location of HNMT in glioma cell line. Collectively, our data provide hint that HNMT is another noval theraptic target for deadly glioma.